ABSTRACT

Charles University in Prague
Faculty of Pharmacy in Hradec Králové
Department of Biochemical Sciences
Titul, Name, Surname of candidate: Bc. Jana Osecká
Titul, Name, Surname of tutor: Doc. RNDr. Lenka Skálová, Ph.D.
Title of a diploma work: **Stability, extraction and metabolism of doxorubicin**

Anthracyclines antibiotics belong among the most effective cytostaticum and the most often used chemotherapeutic drugs. The main representative of this line is doxorubicin (DOX). Wide spectrum of solid tumors and human hematology malignancies react on the therapy of DOX. DOX is the most effective in breast carcinoma therapy. The main unwanted effect of DOX is cardiotoxicity and resistance of medicine. Clinically the most significant effect of DOX is secondary alkohol doxorubicinol (DOXOL), which is not cytostatic effective, but it is more cardiotoxic. In this case inhibition of transformation DOX to DOXOL would lead to reduction of deactivation and cardiotoxicity DOX. The aim of graduation thesis was to contribute to study of metabolism of DOX by testing stability of the water solution DOX and DOXOL during different conditions, optimizing of extraction DOX and DOXOL and testing effect of potential inhibitor of oracin and quercetin to reduction DOX in cytosol from breast tumor cells. It was found out, that DOX is in solution very unstable. These solutions are necessarily to keep in the dark place on temperature 4° C and pH can not rise over 6 and only for the shortest period of time. The acceptable extractive method for DOX and DOXOL is extraction by acetone with saturated $ZnSO_4$. The effectiveness of extraction had valuation higher than 80%. During the study of the metabolism of DOX in cytosol from breast tumor of the cell line, strong inhibitive effect of oracin and quercetin was found out in low concentration. In cell of Ehrlich´s solid tumor the oracin in the high concentration inhibited activity reductas of DOX only little.